

# Exhibit C



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
10903 New Hampshire Avenue  
Document Control Room W-066-0609  
Silver Spring, MD 20993-0002

FEB 11 2011

Ms. Susan Lin  
Manager, Regulatory Affairs  
Ethicon Women's Health & Urology  
Route 22 West  
P.O. Box 151  
SOMERVILLE NJ 08876

Re: K103727  
Trade Name: GYNECARE TVTO-PA Continence System  
Dated: December 21, 2010  
Received: December 22, 2010

Dear Ms. Lin:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above. We cannot determine if the device is substantially equivalent to a legally marketed predicate device based solely on the information you provided. To complete the review of your submission, we require the following:

Clinical Performance Data

In this submission, you provided no human clinical data or literature to support the safety and effectiveness of the GYNECARE TVTO-PA Continence System for treatment of stress urinary incontinence (SUI) resulting from urethral hypermobility and/or intrinsic sphincter deficiency. The subject mesh has a different material composition compared to your proposed predicate device, the GYNECARE TVT Obturator System (K033568). The subject mesh is a 50:50 ratio of PROLENE™ and MONOCRYL™ and is partially absorbable, while the predicate mesh is only PROLENE™ and is non-absorbable. It is unknown what effect the change in material composition will have on the safety and effectiveness of the subject device, and as a result, we believe that clinical data is needed to support its clearance.

1. You state that the rationale for using a partially absorbable material for the TVTO-PA System is that "less permanent material will be implanted in the patient." We believe this statement implies there is a clinical benefit to using the TVTO-PA System in regards to the adverse event rate.

In order to evaluate the effect of the change in material composition on the likelihood of adverse events related to the TVT-O procedure, please provide clinical data evaluating the adverse event rates with the TVTO-PA System compared to those seen with the

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GYNECARE TVT predicate mesh. To obtain this data, please conduct a randomized, controlled, evaluator blinded trial comparing adverse event rates with transobturator placement of the TVTO-PA mesh compared to the GYNECARE TVT mesh. This study should demonstrate that the adverse event rates associated with the TVTO-PA mesh at 12-months post-procedure are non-inferior to those seen with the GYNECARE TVT mesh.

The study should evaluate the following adverse events at both 6 and 12-months:

- Mesh erosion
- Infection
- Pelvic pain
- De novo dyspareunia
- De novo urgency
- Urinary retention
- Groin/thigh pain
- Reoperation due to mesh complications

The primary endpoint and sample size calculation should be based specifically on demonstrating non-inferiority of the TVTO-PA mesh erosion rate at 12-months compared to the predicate mesh erosion rate at 12-months.

2. We believe that data from the published literature and any known clinical studies using the TVTO-PA or similar transobturator sling devices may be acceptable to demonstrate the effectiveness of the TVTO-PA System. However, this is contingent upon how you address the questions surrounding the absorption rate of the MONOCRYL™ component of the subject mesh as described in Question No. 3.

If you are able to adequately demonstrate that the subject mesh is able to maintain adequate mechanical properties while undergoing absorption, (i.e., similar mechanical properties to that of the predicate device), literature data may suffice to address the question of device effectiveness. This data should demonstrate the effectiveness of the TVTO-PA Continence System for treating patients with SUI due to (1) hypermobility and (2) intrinsic sphincter deficiency.

If the subject mesh does not meet the stated requirements, then we believe effectiveness should also be addressed through the clinical study requested in Question No. 1. In that case, we recommend you use the draft FDA Guidance Document titled “Clinical Investigations of Devices Indicated for the Treatment of Urinary Incontinence” issued on September 19, 2008 in designing the effectiveness component of the study.

We strongly recommend that you submit your proposed study plan in response to Question No. 1 and literature and/or performance data in response to Questions No. 2-3 as a pre-IDE submission

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for our review and comment prior to initiating the requested clinical study.

MONOCRYL™ Resorption Rate

3. On pages 38-39 of your submission, you state that based on implantation studies in rats, MONOCRYL™ suture retains approximately 50-60% of its original tensile strength 7 days post-implantation, 20-30% 14 days post-implantation, and 0% at 21-28 days post-implantation. You also state that MONOCRYL™ suture is completely absorbed between 91 and 119 days.

These statements are not supported by the implantation study you completed to assess biocompatibility, titled “Local Tissue Response and Absorption Study of Scion PA Device following Intramuscular Implantation in Rabbits for 14, 28, 91, 180, and 270 Days.” On page 10 of 23 of this study report you state, “the absorbable components of the test and control articles were not absorbed at 14 or 28 days post-implantation, but had evidence of absorption at 91 days post-implantation. At 119 days post-implantation, .... the absorbable components of the test mesh ... were considered completely absorbed.”

As a result, the degradation rate and time to complete resorption of the MONOCRYL™ component of the subject mesh is unclear. It is possible that the discrepancy between the two studies is the result of one or more of the following factors:

- Animal model (rat versus rabbit)
- Implantation site (subcutaneous (?) versus intramuscular)
- Test article (suture versus subject mesh)

Please address the discrepancy between the two studies, and please provide evidence verifying the degradation rate and time to complete resorption of the MONOCRYL™ component of the subject mesh in a human model in the target tissue. Please also describe how the rate of tissue ingrowth during the resorption time frame is sufficient to overcome the progressive loss of tensile strength of the subject mesh during this period.

Mechanical Performance Testing

4. You completed tensile testing on baseline samples of the GYNECARE TVTO-PA surgical mesh. Although the results of this testing are acceptable, this test alone is not sufficient to fully characterize the mechanical behavior of the subject surgical mesh. In addition, you did not provide all the performance data recommended in the FDA Guidance Document “Guidance for the Preparation of a Premarket Notification Application for a Surgical Mesh” issued on March 2, 1999.

Therefore, please provide the protocol and results of testing evaluating the following characteristics:

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- Dimensional Analysis (mesh thickness, pore size, mesh density)
- Tensile Strength to Failure
- Mesh Stiffness
- Burst Strength
- Tear Resistance
- Pullout Strength of Attachment Lines to Mesh
- Pullout Strength of Attachment Lines to Tube Receptacle
- Removal of Plastic Sheath

The dimensional analysis, mesh stiffness, burst strength, tear resistance, and tensile strength to failure should be evaluated at baseline and following complete resorption of the MONOCRYL™ component of the subject mesh. In addition, please evaluate the tensile strength to failure at incremental percentages of MONOCRYL™ resorption.

#### In Vivo Biomechanical Evaluation

5. You conducted an in vivo biomechanical evaluation of the GYNECARE TVTO-PA surgical mesh in rabbits to address the potential loss in mesh strength as the MONOCRYL™ component degrades and is absorbed. You evaluated the fixation strength of the subject mesh in the surrounding tissue at 7, 14, and 28 days post-implantation. The fixation strength was assessed by subjecting the mesh to a force of 164 grams. A sample was considered a “pass” if no slippage or dislocation of the sample from its in situ position relative to the starting location or fascia was observed.

We have the following concerns regarding this study:

- a. As described in Question No. 3, the absorption rate of the MONOCRYL™ component of the subject mesh is unknown. Therefore, it is unclear if 28 days is the appropriate length of time for this study. Based on the results of the rabbit implantation study, if no resorption occurs at 28 days, then a significant drop in tensile strength should not be observed at 28 days. Please address this issue.
- b. It is unclear why you chose to evaluate if the test samples could subject a specific maximum force (164 grams) rather than evaluating the test samples out to failure. By evaluating the test samples out to failure, we could have observed if there was any progressive loss in tensile strength. Please justify your method of evaluation.
- c. You cited the Lin et al (2005) study to justify the 164 gram force to which the test samples were subject. You state that 164 grams of force is “more than 100 times greater than the highest tension sustained by a fascial sling following pubovaginal sling surgery.” Based upon our review of this paper, it is unclear what value you used to calculate the 164 gram fixation force. Please provide this information.

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Predicate Device Comparison

6. Your proposed predicate device is the GYNECARE TVT Obturator System (K033568). Although the subject device and your proposed predicate device have the same intended use, they have different technological characteristics, as a result of their different material composition. The subject mesh is a 50:50 ratio of PROLENE™ and MONOCRYL™, while the predicate mesh is only PROLENE™. Therefore, please include another cleared surgical mesh with a similar material composition (e.g., ULTRAPRO Partially Absorbable Lightweight Mesh (K033337) indicated for hernia repair and the GYNECARE PROLIFT+M Pelvic Floor Repair System (K071512) indicated for pelvic organ prolapse repair) as a second predicate device. Please also revise your substantial equivalence discussion accordingly.

Device Description

7. You state that the GYNECARE TVTO-PA surgical mesh is fabricated from PROLENE™ and MONOCRYL™ monofilaments knitted together. Please describe in greater detail how the two mesh components are knitted together, (i.e., is the subject mesh essentially a layer of PROLENE™ mesh on top of a layer of MONOCRYL™ mesh or are the two components intertwined to form a single layer of mesh?).
8. The GYNECARE TVTO-PA surgical mesh includes polypropylene attachment lines. These attachment lines are not found in the predicate GYNECARE TVT Obturator System. Please state the purpose of the attachment lines, and please explain why you chose to make this modification.
9. Unlike the predicate GYNECARE TVT Obturator System, the Helical Passers provided with the subject device will not come pre-attached to the surgical mesh. In evaluating the samples of the subject device you provided, it appears that it may be difficult to push the tube receptacles along the curve of the Helical Passer guide. Please address the difficulty of attaching the mesh to the Helical Passer in the operating environment.

Sterilization

10. You state that the ethylene oxide (EO) and ethylene chlorhydrin (ECH) residuals will comply with the maximum limits specified in ISO 10993-7:2008 for limited contact or permanent contact medical devices as appropriate for the component. Please provide data confirming that the EO and ECH residuals are no greater than 4 mg and 9 mg respectively for the Helical Passers and Atraumatic Winged Guide and any greater than 2.5 g /lifetime and 10 g /lifetime respectively for the surgical mesh.

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Shelf Life

11. You propose a 12-month shelf life for the GYNECARE TVTO-PA Continence System based on the results of accelerated aging testing conducted at 50°C for 1.2 and 2.3 months. You state these conditions are the respective equivalent of 7 and 13 months of real-time aging. Please explain how you determined the real-time equivalent of your accelerated aging conditions.
12. You did not provide the results of the accelerated aging testing described in Question No. 11 but state that this testing will be completed prior to marketing the subject device. This is not acceptable, as this data needs to be reviewed prior to clearance. Therefore, please provide the results of accelerated aging testing supporting your proposed 12-month shelf life. The results of this testing should demonstrate that the subject device maintains its mechanical integrity and sterility over this time frame. Please evaluate the mechanical integrity of the device following aging as described in Question No. 4 of this letter.
13. Please provide your protocol to evaluate shelf-life following real-time aging for review. Real-time aging should be completed to verify the results of accelerated aging.

Labeling

14. Please provide a draft copy of the outer box label and the package label for the GYNECARE TVTO-PA for review.
15. Please note that a comprehensive review of your draft package labeling has not been completed and changes to this document will be requested as we continue our review of this submission. However, please be aware that the package labeling should reference cure rates for transobturator slings in treating SUI due to (1) hypermobility and (2) intrinsic sphincter and should include a description of the types and occurrence rates of associated adverse events.

510(k) Summary

16. Please revise your 510(k) Summary as follows:
  - a. Please state that the subject device is classified under product code OTN (mesh, surgical, gynecologic, for stress urinary incontinence, female).
  - b. Please include the additional predicate device requested in Question No. 6.
  - c. Please include a description of the additional performance testing requested in this letter.

Please provide a revised 510(k) Summary accordingly. Please note that changes to your 510(k) Summary will be requested as we continue our review of this submission.

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Administrative Issues

17. Please provide a completed ClinicalTrials.gov Data Bank Form (Form 3674) in accordance with your response to Question No. 1 of this letter. This form can be found at the following web page: <http://www.fda.gov/opacom/morechoices/fdaforms/FDA-3674.pdf>.

The deficiencies identified above represent the issues that we believe need to be resolved before our review of your 510(k) submission can be successfully completed. In developing the deficiencies, we carefully considered the statutory criteria as defined in Section 513(i) of the Federal Food, Drug, and Cosmetic Act (Act) for determining substantial equivalence of your device.

You may not market this device until you have provided adequate information described above and required by 21 CFR 807.87(l), and you have received a letter from FDA allowing you to do so. If you market the device without conforming to these requirements, you will be in violation of the Act. You may, however, distribute this device for investigational purposes to obtain clinical data if needed to establish substantial equivalence. Clinical investigations of this device must be conducted in accordance with the investigational device exemption (IDE) regulations (21 CFR 812).

If the information, or a request for an extension of time, is not received within 30 days, we will consider your premarket notification to be withdrawn and your submission will be deleted from our system. If you submit the requested information after 30 days it will be considered and processed as a new 510(k)(21 CFR 807.87(l)); therefore, all information previously submitted must be resubmitted so that your new 510(k) is complete. For guidance on 510(k) actions, please see our guidance document entitled, "FDA and Industry Actions on Premarket Notification (510(k)) Submissions: Effect on FDA Review Clock and Performance Assessment" at <http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM089738.pdf>

If the submitter does submit a written request for an extension, FDA will permit the 510(k) to remain on hold for up to a maximum of 180 days from the date of the additional information request.

The purpose of this document is to assist agency staff and the device industry in understanding how various FDA and industry actions that may be taken on 510(k)s should affect the review clock for purposes of meeting the Medical Device User Fee and Modernization Act. .

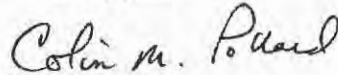
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The requested information, or a request for an extension of time, should reference your above 510(k) number and should be submitted in duplicate to:

U.S. Food and Drug Administration  
Center for Devices and Radiological Health  
Document Mail Center – WO66-G609  
10903 New Hampshire Avenue  
Silver Spring, MD 20993-0002

If you have any questions concerning the contents of the letter, please contact Ms. Sharon Andrews at (301) 796-6650. If you need information or assistance concerning the IDE regulations, please contact the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or at (301) 796-7100, or at its Internet address <http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>.

Sincerely yours,



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